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Unusual association of diseases/symptoms

Actinobacillus endocarditis associated with hypertrophic cardiomyopathy

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Summary

Infective endocarditis can be associated with complex clinical presentations, sometimes with a difficult multi-disciplinary management. *Actinobacillus actinomycetemcomitans* belongs to the *Haemophilus* species, *Actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella* species group, responsible for 5% to 10% of infective endocarditis in native heart valves. These organisms have slow fastidious growth pattern, often associated with negative cultures, and cause systemic embolism with abscess formation. The authors present the case of a 59-year-old man, admitted due to fever of unknown origin, with a personal history of obstructive hypertrophic cardiomyopathy and recent dental manipulation. The diagnosis of mitral valve's endocarditis was established after a transoesophageal ecocardiography, with a late isolation of *A actinomycetemcomitans* in blood culture. Despite the institution of antibiotic therapy, the patient suffered from multiple episodes of septic embolism: skin, mucosae, cerebral abscesses, spondylodiscitis and uveitis. He was submitted to heart surgery with miectomy and replacement of the native mitral valve by a mechanical prosthesis, while on antibiotics.

BACKGROUND

Infective endocarditis is not a common entity, yet it remains a severe and potentially lethal disease.[1]

In the clinical case presented, we underline the diagnostic difficulty, despite the high level of clinical suspicion, in accordance with the great capacity of *Actinobacillus actinomycetemcomitans* for systemic embolism. Aside the aetiologic agent of endocarditis, in this case, being infrequent we stress the rare association with hypertrophic cardiomyopathy and the organs targeted by systemic embolisation, as well as the need of a multi-disciplinary approach to deal with the systemic involvement.

CASE PRESENTATION

A 59-year-old Caucasian man with a history of fever for 2 weeks was admitted in the Internal Medicine Ward. The fever had maximal temperatures of 38°C, two peaks per day, mostly in the afternoon, and a good response to antipyretics; it was associated with diaphoresis, anorexia, 3 kg weight loss, ocular redness with blurred vision in the left eye, progressive inflammatory lumbar pain (with a need of gait aids) and worsening rectal bleeding. In that length of time, he was diagnosed with anterior uveitis and began topical therapy with steroids and anticholinergic drugs. Of note, he had a history of dental surgery 3 weeks before admission to the hospital.

The patient had a known history of arterial hypertension, obstructive hypertrophic cardiomyopathy (1995), ischaemic stroke without neurological sequelae (2006), cholecystectomy for biliary lithiasis (1992), lumbar disc herniation and haemorrhoids (waiting surgical correction).

On clinical examination, the patient presented with skin and mucosal pallor, left eye redness and multiple dental cavities; cardiac auscultation with rhythmical heart sounds and a systolic murmur, III/VI in the mitral area and another one, II/VI, in the aortic area; the Lasègue test was positive on both sides with painful lumbar spinous processes palpation.

The initial investigation revealed normocytic normochromic anaemia (haemoglobin of 12 g/dl), raised inflammatory parameters, acute renal failure and active urinary sediment (table 1). The ECG showed sinus rhythm (HR: 110 bpm) with voltage criteria for left ventricle hypertrophy. The chest radiography was unremarkable.

Fever of unknown origin was assumed, with the most likely infectious causes being acute spondylodiscitis, endocarditis, brucellosis or tuberculosis; an autoimmune aetiology, like systemic vasculitis or spondyloartropathy with inflammatory bowel disease, were also considered.

Serologic, immunologic, blood and urine cultures were negative. The transthoracic echocardiogram did not reveal vegetations and the x-ray and CT study of the lumbar spine and sacro-iliac joints, as well as the thoracoabdominopelvic CT were unremarkable.

The transoesophageal echocardiogram showed one globular vegetation (12 mm in diameter) on the anterior mitral leaflet (figure 1); severe mitral regurgitation (III/IV); aortic valve with normal morphology and mild regurgitation. The left ventricular outflow tract gradient was in the range of 30–35 mm Hg by trans thoracic echocardiogram. The patient was started on vancomycin (1g qd intravenous), due to alleged penicillin allergy, and gentamycin (120 mg qd intravenous, according to his creatinine clearance). On the 14th day as inpatient, we were notified about the growth of a gram-negative *Haemophilus* species, *Actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella* species (HACEK) group organism, with the isolation of *A actinomycetemcomitans* on the 17th day, with a subsequent substitution of vancomycin for ceftriaxone (2g qd intravenously).

Table 1 Relevant laboratory parameters

Parameter	Value		
	In the beginning	**Two weeks of antibiotic therapy**	**Two weeks after surgery and 6 weeks of antibiotic therapy**
Haemoglobin	12 g/dl	9.6 g/dl	10.2 g/dl
Leucocytes/neutrophils	12100 mm^3; 90.7%	12300 mm^3; 87.2%	5900 mm^3; 85.7%
Urea	116.6 mg/dl	27.4 mg/dl	44.6 mg/dl
Creatinine	3.2 mg/dl	1.3 mg/dl	1.6 mg/dl
C reactive protein	27.4 mg/dl	4.6 mg/dl	1.2 mg/dl
ESR	31 mm/h	66 mm/h	58 mm/h
Urinary sediment			
Proteinuria	100 mg/dl	Negative	Negative
Eritrocituria	+2	Negative	Negative
Leucocituria	25 μl	Negative	Negative

ESR, erythrocyte sedimentation rate.

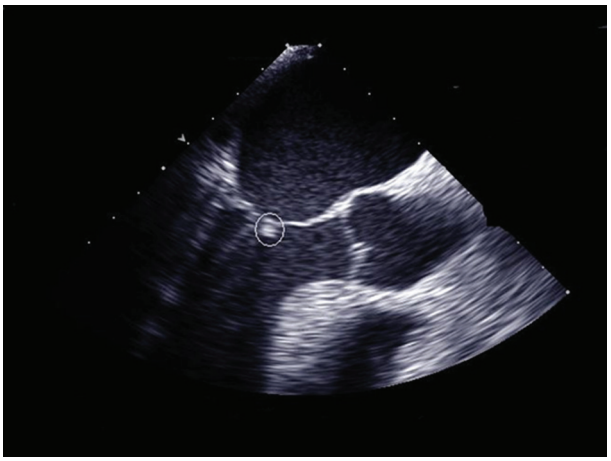

Figure 1 Transoesophageal echocardiogram.

Figure 2 Left-eye hypopion.

Despite the antibiotic prescription, the patient remained febrile, with signs of systemic embolism: worsening uveitis, with hypopion (figure 2), Osler nodules and Janeway lesions on his palms and plants (figure 3), palate petechias and splinter subungueal haemorrhages. Due to worsening of lumbar pain, he underwent MRI that revealed an acute spondylodiscitis in L4/L5 level (figure 4). He had orthopaedic surgery, with vertebral cleansing and stabilisation; the gram and cultural examinations (bacterial and mycobacteria) of the removed material were negative. Systemic embolism, in spite of the absence of focal neurological signs, dictated the need for a head CT scan, which revealed several images suggestive of white matter abscesses, confirmed by MRI: multiple abscesses of small dimensions (the biggest with 5 mm) in the white frontal and temporal matter on the right side and white parietal and posterior frontal matter on the left side.

The case was discussed in a joint meeting with the cardiology and cardiothoracic surgeons, both choosing to postpone the surgery until antibiotic sterilisation of the valve.

The decision to proceed with a kidney biopsy was suspended after progressive recovery of kidney function. The colonoscopy was postponed, due to the algic complaints and the position intolerance.

After re-adjusting the antibiotic therapy, with replacement of ceftriaxone for ciprofloxacin (750 mg twice daily per os), the patient remained afebrile with symptomatic improvement and improving laboratory inflammatory parameters (table 1). He had cardiac surgery after a 6 week course of antibiotic, with replacement of the native mitral valve by a mechanical prosthesis and a morrow myectomy procedure; afterwards, he was started on anticoagulation. Unfortunately, the valve removed was not sent for culture. The surgery was performed in another hospital.

OUTCOME AND FOLLOW-UP

He completed an 8 weeks course of antibiotics as an inward patient and was discharged home with a recommendation for a total of 24 weeks antibiotic therapy with ciprofloxacin for the spondylodiscitis (table 1). The patient had a full recovery, with disappearance of the cerebral abscesses and orthopaedic surgery for the vertebral column.

DISCUSSION

Diagnosing infective endocarditis can be difficult, since this disease often has a disguised course. 20%–30% of

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cases do not have previous valvular lesions. Men are more frequently affected than women.[2]

Mitral endocarditis complicating hypertrophic cardiomyopathy occurs predominantly on the left ventricular aspect of the anterior mitral valve leaflet in the presence of outflow tract obstruction. It is a rare condition and the estimated cumulative 10 year probability of developing endocarditis in patients with obstruction is <5%.[3 4]

Echocardiographic studies and blood cultures are the cornerstone of the diagnosis. Duke's criteria are useful but are not substitutes to clinical sense.[5]

Once excluded individuals with a history of antibiotic prophylaxis, the rate of culture-negative infective endocarditis averages 5%. These patients might be infected by organisms known for a slow or fastidious growth in usual culture systems (over 6 days), like piridoxin requiring *Streptococci*, gram negative coccobacilli from the HACEK group *Corynebacterium spp., Neisseria gonorrhoeae* and *anaerobes*.[1]

The use of broad-spectrum PCR provides a significant improvement in the capability to detect difficult-to-culture organisms and even dead bacteria.[6]

Systemic embolism occurs in up to 20%–50% of infective endocarditis, diminishing to 6%–21% after the beginning of antibiotics; it is more frequent in the first two weeks of antibiotic treatment.[5]

Up to 65% of embolisms target the central nervous system, having neurological complications in about 20%-40%: stroke, infectious aneurysms, intracranial haemorrhage, meningeal processes, seizures, non-focal symptoms, encephalopathy and immune phenomena.[7 8]

The majority of ophthalmic manifestations of bacterial endocarditis result from microembolisation of bacteria or debris from the damaged valve into the retinal and choroidal circulations.[12 13]

Spondylodiscitis is seldom reported, mostly in case reports. The frequency depicted in literature is contradictory (0.6% to 15%).[8–11]

Kidney failure is a frequent complication of infective endocarditis, affecting about 30% of patients, carrying with it a bad prognosis. Most of the times, aetiology is

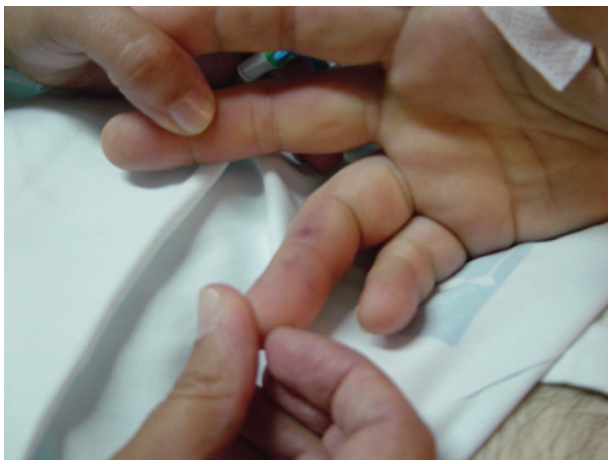

Figure 3 Janeway lesions.

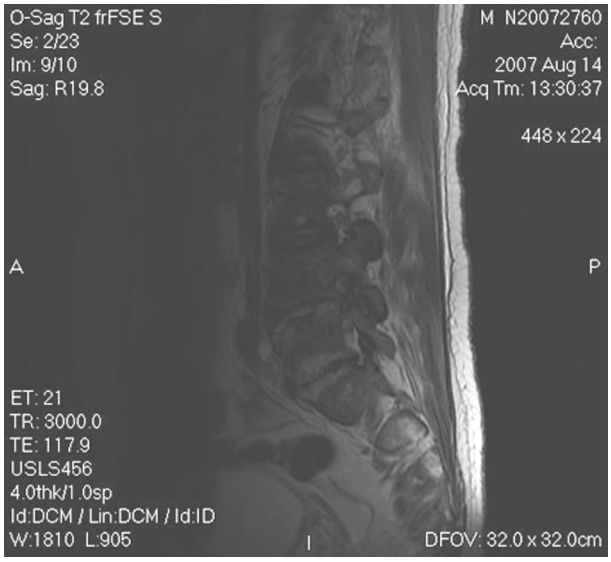

Figure 4 Lumbar-sacral column MRI.

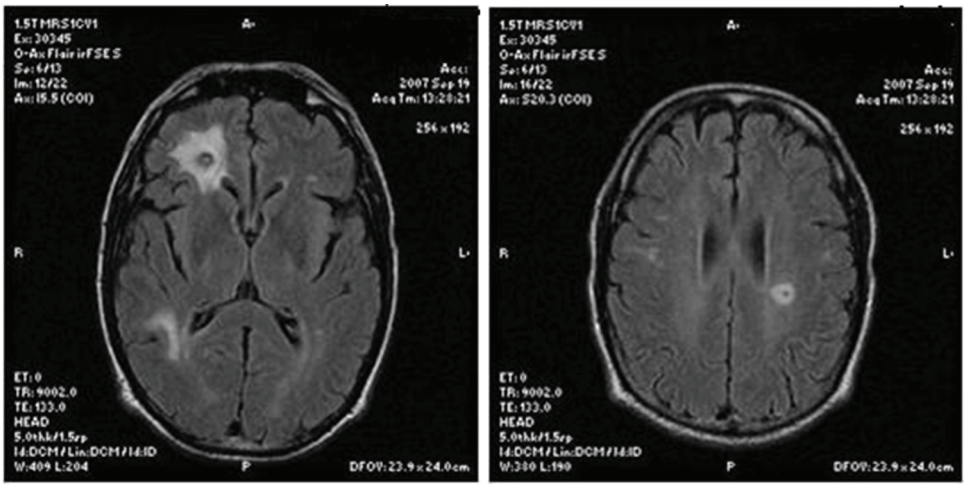

Figure 5 Head MRI, with multiple abcesses of small dimensions (the biggest with 5 mm) in the white mater (frontal and temporal on the right hemisphere and parietal and posterior frontal on the left hemisphere). Perilesional vasogenic oedema of the white matter, without deformation of the sulci and ventricular contour.

multifactorial, and can be due to immune complex or vasculitic glomerulonephritis, renal infarction, haemodynamic changes or nephrotoxicity.[5]

The HACEK group is responsible for 5%–10% of cases of infective endocarditis involving native valves.[3] These organisms usually cause subacute disease and are the most common gram negative organisms isolated from patients with infective endocarditis. Complications may include massive arterial emboli and congestive heart failure (50%). These complications are due to the intrinsic properties of the organisms themselves, the significant delay in diagnosis, or a combination of these factors. Sixty per cent of cases of HACEK infective endocarditis are associated with various types of dental pathology. Mortality range from 10%–40%.[4 14]

Among the bacteria of the HACEK group, *A actinomycetemcomitans* is the organism involved most commonly in infective endocarditis. It occurs most commonly in men, with a pre-existing cardiopathy and the most frequent valve involved is the aortic valve.[15]

A actinomycetemcomitans is a fastidious, gram-negative coccobacillus that forms part of the normal oral flora and can gain entry to the vascular compartment via dental infection, dental procedures or spontaneous bacteraemia resulting from mastication.[16]

In addition to endocarditis, *A actinomycetemcomitans* may cause head and neck infections, brain abcesses, pneumonia, soft tissue infections and urethritis.[16]

A actinomycetemcomitans is generally more susceptible to third-generation cephalosporins than to penicillin: ceftriaxone (2 g intravenously q24 h) for a minimum of 4 weeks for native-valve endocarditis or 6 weeks for prosthetic-valve endocarditis. Ciprofloxacin (750 mg PO q12 h or 400 mg intravenously q12 h) is another alternative to ceftriaxone.[4 14]

A brief review was made based on the Medical Literature Analysis and Retrieval System Online search using the Pubmed database. The search of actinobacillus endocarditis associated with hypertrophic cardiomyopathy revealed no references. The key-words actinobacillus endocarditis revealed 27 references (103 cases): 20 were in English, two in French, two in Spanish, one in Japanese, one in German and one in Dutch. Moreover, all full references that described human cases found since the first case description in 1964 were recorded.

Learning points

- Infective endocarditis remains a diagnostic challenge, sometimes originating complex and difficult to manage clinical pictures, with a need of multi-disciplinary approach.
- HACEK microorganisms must be kept in mind, specially when facing an infectious disease with repeated negative cultures.
- The institution of antibiotic therapy is of the essential importance in infective endocarditis, markedly decreasing the rate of systemic embolism, specially in the case of more aggressive microorganisms, like *A actinomycetemcomitans.*

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Cordero A,** Escoto V, Lopes L. Endocardite por Bartonella: um caso de endocardite com culturas negativas. *Revista da Sociedade Portuguesa de Medicina Interna* 2008;**15**:186–191.
2. **Borges S,** Costa A, Bourbon F, *et al*. Brucelose com Endocardite. *Revista da Sociedade Portuguesa de Medicina Interna* 2009;**16**:86–92.
3. **Morgan-Hughes G,** Motwani J. Mitral valve endocarditis in hypertrophic cardiomyopathy: case report and literature review. *Heart* 2002;**87**:e8.
4. **Brush JL**. Infective endocarditis. Emedicine (WebMD). 2009. Available from: URL: http://emedicine.medscape.com/article/216650-overview. (accessed 31 March 2011).
5. Grupo de Trabalho da European Society of Cardiology (ESC) para a Prevenção, o Diagnóstico e o Tratamento da Endocardite Infecciosa. Recomendações para a prevenção, o diagnóstico e o tratamento da endocardite infecciosa (nova versão 2009). *Revista da Sociedade Portuguesa de Cardiologia* 2010;**29**:845–890.
6. The Task Force on Infective Endocarditis of the European Society of Cardiology. Guidelines on Prevention, Diagnosis and Treatment of Infective Endocarditis. *European Heart Journal* 2004;**25**:267–276.
7. **Ahmed A,** Hargrave K, Fisher JR, *et al*. Neurological Sequelae of Infectious Endocarditis. Emedicine (WebMD). 2009. Available from: URL: http://emedicine.medscape.com/article/1165712-overview. (accessed 31 March 2011).
8. **Luz A,** Castro A, Ribeiro R, *et al*. Endocardite bacteriana a estreptococos do grupo viridans associada a espondilodiscite. *Revista da Sociedade Portuguesa de Cardiologia* 2004;**23**:723–728.
9. **Le Moal G,** Roblot F, Paccalin M, *et al*. Clinical and laboratory characteristics of infective endocarditis when associated with spondylodiscitis. *Eur J Clin Microbiol Infect Dis* 2002;**21**:671–5.
10. **Weber M,** Gubler J, Fahrer H, *et al*. Spondylodiscitis caused by viridans streptococci: three cases and a review of the literature. *Clin Rheumatol* 1999;**18**:417–21.
11. **Morelli S,** Carmenini E, Caporossi AP, *et al*. Spondylodiscitis and infective endocarditis: case studies and review of the literature. *Spine* 2001;**26**:499–500.
12. **Reese LT,** Shafer D. Retinal embolization from endocarditis. *Ann Ophthalmol* 1978;**10**:1655–7.
13. **Schocket S,** Braver D. Cilioretinal artery occlusion in a patient with suspected subacute bacterial endocarditis. *South Med J* 1970;**63**:1–4.
14. **Humphrey P,** Kelly MK, Barnett G, *et al*. HACEK Group Infections. Emedicine (WebMD). 2009. Available from: URL: http://emedicine.medscape.com/article/218158-overview. (accessed 31 March 2011).
15. **Paturel L,** Casalta JP, Habib G, *et al*. Actinobacillus actinomycetemcomitans endocarditis. *Clin Microbiol Infect* 2004;**10**:98–118.
16. **Shles A,** Wolach B, Levi A, *et al*. Actinobacillus actinomycetemcomitans endocarditis in a 1.5 year old toddler. *BMJ Case Reports* 2010; doi: 10.1136/bcr.11.2009.2462.